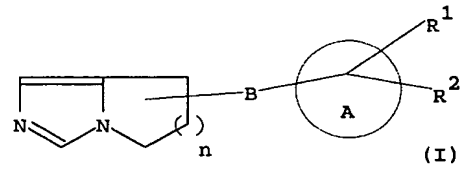
97-231178/21 B02 YAMA 95.09.07
YAMANOUCHI PHARM CO LTD *JP 09071586-A
95.09.07 95JP-230132 *(97.03.18)* C07D 487/04, A61K 31/415, 31/435, 31/44, 31/495, 31/50, 31/505, 31/535, 31/55, C07D 471/04

New bi:cyclic fused imidazole derivs - used as aldosterone biosynthesis inhibitors, e.g. for treating chronic or congestive heart failure

C97-074386

Bicyclic fused imidazole derivs. of formula (I) and their salts are new.



(I)

A = 5-6 membered unsatd. heterocyclic ring contg. 1-4 N or S;
B = a bond or opt. OH-substd. alkylene;
R^1, R^2 = H, halogen, lower alkyl, lower alkoxy, NR^3R^4, $S(O)_mNR^5R^6$

B(6-D7, 14-D2A1, 14-D3, 14-E10, 14-F1B, 14-L6, 14-N10, 14-N17) .6

or morpholinyl;
R^3-R^5 = H or lower alkyl;
m = 1 or 2.

USE

(I) are aldosterone biosynthesis inhibitors (claimed) used for treatment of chronic heart failure, myocardial fibrosis, hyperaldosteronism, hypokalaemia, alkalosis, polyuria, renal or intrinsic hypertension, congestive heart failure, left ventricular failure, oedema, cirrhosis, cardiac hypertrophy or disorders of the skin and digestive organs.

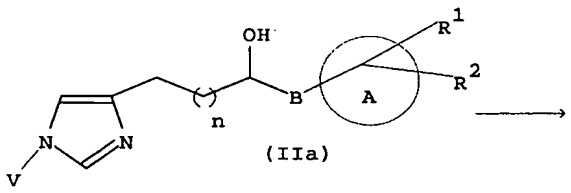
Dosage is 0.1-100 (pref 0.1-10) mg/day in one or divided oral doses, or 0.1-100 mg/day by parenteral administration.

ADVANTAGE

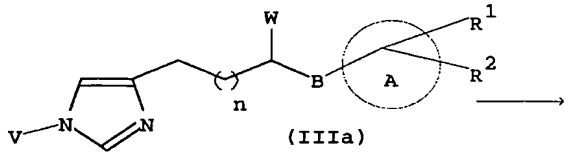
(I) specifically inhibit the cytochrome P450 C18 enzyme. They show *in vivo* inhibitory activity to aldosterone prodn at a dose of 10 mg/kg or lower.

PREPARATION

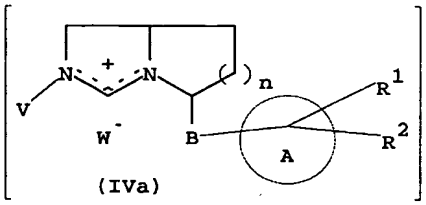
(I) are prepd. e.g. as follows:



(IIa)

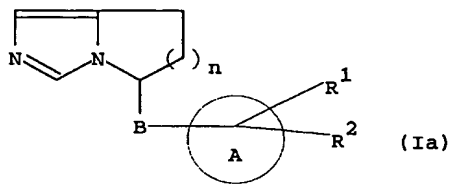


(IIIa)



(IVa)

97-231178/21



(Ia)

V = H, trityl, acetyl, $CON(Me)_2$ or $SO_2N(Me)_2$;
W = Cl, Br, mesyloxy or tosyloxy. (RMH)
(21pp079DwgNo.0/0)